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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,122	12/05/2003	James A. Williams	D-2939CIPCONDIV2	9828

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 02/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/729,122	WILLIAMS, JAMES A.	
	Examiner	Art Unit	
	Ginny Portner	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/5/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-24 have been canceled; New Claims 25-38 have been submitted.

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 25-26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2 of U.S. Patent No. 5,919,665. Although the conflicting claims are not identical, they are not patentably distinct from each other because the allowed claims are directed to a species of invention of the instantly claimed genus of botulinum toxins, wherein the allowed species is directed to a fusion protein that comprises SEQ ID NO 23 and 28 that is fused together with a non-toxin protein sequence and the instantly claimed invention is not claimed to be a fusion protein but is a recombinant botulinum toxin that comprises SEQ ID NO 23 and a portion of SEQ ID NO 28, along with a non-toxin protein sequence which is not required to be fused together with recombinant botulinum toxin, and therefore may be conjugated or linked by other means other than that defined by the recitation of "fusion protein". The allowed species anticipates the instantly claimed genus of botulinum toxins.

Information Disclosure Statement

The information disclosure statement filed December 5, 2005 has been considered.

Claim Objections

1. Claims 25-38 are objected to because of the following informalities:

Claim 28 recites the phrase "wherein the toxin is in a solution"; the claim should recite the phrase ----further comprising----, or claimed as a composition comprising the toxin and a solution.

Claims 25-38 recites the phrase "comprise SEQ ID NO 28"; this sequence is the entire coding sequence for the light and heavy chains of botulinum toxin, and therefore is not a portion. The definition of "portion" recited in all of the claims is not met through the recitation of the complete sequence for the botulinum toxin. No portions are recited in the claims through the recitation of "comprise SEQ ID NO 28". The claim language and the recitation of SEQ ID NO 28 are inconsistent with the meanings of the terms recited. Appropriate correction is required.

Claim Rejections - 35 USC 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Please Note: In light of the claimed invention requiring the recombinant botulinum toxin to comprise the recited portions the claimed toxins read on isolated complete botulinum toxins.

Additionally the recitation of the term "recombinant" is being read as a process limitation, and the claimed toxin reads on the naturally occurring toxins absent claiming distinguishing characteristics that differ from that which occurs in nature, as no structural differences are encompassed by what is now claimed from that which would be present in an isolated botulinum toxin produced by natural sources.

3. Claims 25-38 are rejected under 35 U.S.C. 102(e) as being anticipated by Dolly et al (US Pat. 6,203,794, effective filling date May 31, 1994) as evidenced by Ledoux et al (1994).

Dolly et al disclose the instant claimed invention directed to a recombinant botulinum neurotoxin (see Dolly et al, col. 2, lines 25-36), wherein the botulinum toxin is botulinum toxin A, B, C, D, E, F and G (see Dolly et al, col. 7, lines 18-30; col. 41, claims 2-3).

(Instant claims 25-26; 32) The botulinum toxin comprises a light chain portion (see Dolly et al, col. 8, line 2; see Dolly et al, claims 1-3; col. 24, lines 62-65; Example 15), a heavy chain targeting portion and an internalizable portion (see Dolly et al, claim 4, and col. 5, lines 12-14) which are equivalent portions to the C-terminal and N-terminal functions of a botulinum heavy chain.

(Instant claim 27; 34) The botulinum toxin is claimed as a pharmaceutical composition (see Dolly et al claim 4) and is in solution with a pharmaceutically acceptable excipient (see Dolly et al, col. 41, lines 66-67).

(Instant claim 28; 33, 35) The recombinant botulinum toxin is expressed using a maltose binding protein (see col. 17, lines 29-39) expression vector (see Dolly et al, for example: col. 3, lines 54-66) and would therefore evidence a specific solubility conferred by the expression vector fusion protein.

(Instant claim 29-30; 37-38) The C-terminal and N-terminal portions of the heavy chain are bonded one to the other (see Figure 1B) .

(Instant claim 31; 36) The light chain and N-terminal of the heavy chain are bonded to each other (see figure 1B). No distinguishing characteristics have been set forth in the claims to show that the claimed product by process "recombinant" limitation would not be the same or equivalent heavy chain obtained by a different process, specifically purified from natural sources.

The botulinum toxin is disclosed to be mutated through the addition of a non-toxin sequence, specifically a "cysteine" at the N-terminal of the light chain (see Dolly et al, col. 12, lines 55-61). An additional embodiment disclosed is the expression of the recombinant light chain as a fusion protein that comprises "a non-toxin protein sequence" that is cleavable by Factor Xa (see Dolly et al col. 28, lines 59-64; figure 1A) or is a GST fusion protein (see Dolly et al, Example 21, col. 31).

4. Dolly et al anticipates the instantly claimed invention as now claimed, in light of the evidence Ledoux et al provides that defines botulinum toxins to be water soluble proteins (see abstract, page 1095).

Conclusion

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. These references will be applied against amended claims if necessitated by amendment.

6. Bigalke et al (US Pat. 6,822,076) is cited to show hybrid botulinum toxins that comprise an IgE binding domain.

7. Dertzbaugh (US Pat. 6,287,566) is cited to show compositions that comprise protective portions and neutralizing portions of botulinum toxin light and heavy chains.

8. Foster et al (US Pat, 6,395,513 ; 5,989,545) are cited to show botulinum toxin compositions (see claim 5).

9. Gil et al (US Pat. 6,787,517) is cited to show a botulinum toxin agent.

10. Johnson et al (US Pat. 6,444,209; 5,939,070) is cited to show hybrid botulinum neurotoxins that include recombinant toxins.

11. Montal et al (US Pat. 5,837,265) disclose modified B and E botulinum toxins that comprise both a light chain and a heavy chain, the heavy chain comprising both the N- and C-terminal portions (see col. Col. 7, lines 1-59; col. 8, lines 18-20 and claims 3, 7, 11 and 15). The modified toxins were formulated into a pharmaceutical composition and would therefore be in a solution, such as saline (see col. 8, line 51), or combined with a non-toxin protein sequence (see col. 9, lines 32-38 "polypeptides, proteins, amino acids" and lines 45-46).

12. Murphy (US Pat. 5,965,406) is cited to show hybrid botulinum neurotoxins (see all claims).

13. Simpson et al (US Pat. 6,051,239) is cited to show a modified botulinum toxin (see claims).

14. Uhr et al (US Pat. 4,664,911) is cited to show immunotoxins that employ toxin B chain moieties.

15. Zdanovsky (US Pat. 6,214,602) is cited to show recombinant clostridial botulinum toxin light and heavy chain proteins together with an affinity tag (see claims 1-6).

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (571) 272-0862. The examiner can normally be reached on M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Vgp
February 7, 2005

L. F. Smith

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